

This listing of claims will replace all prior versions and listing of claims in the application:

Listing of Claims

1-28. (cancelled)

29. (previously submitted) The formulation of claim 48 wherein the opioids in the formulation consist of alfentanil and morphine.

30. (original) The formulation of claim 29 containing alfentanil in a concentration of from 300 to 6700 mcg/ml.

31. (original) The formulation of claim 29 wherein the concentration of alfentanil, and amount and particle size of the formulation delivered from the device, is selected so that from 100 to 500 mcg/min of alfentanil is deposited in the lungs during inhalation.

32. (original) The formulation of claim 31 wherein the concentration of alfentanil, and amount and particle size of the formulation delivered from the device, is selected so that about 250 mcg/min of alfentanil is deposited in the lungs during inhalation.

33. (original) The formulation of claim 29 containing morphine in a concentration of from 650 to 13350 mg/ml.

34. (original) The formulation of claim 28 wherein the concentration of morphine, and amount and particle size of the formulation delivered from the device, is selected so that from 100 to 2000 mcg/min of morphine is deposited in the lungs during inhalation.

35. (original) The formulation of claim 34 wherein the concentration of morphine, and amount and particle size of the formulation delivered from the device, is selected so that from 200 to 1000 mcg/min of morphine is deposited in the lungs during inhalation.

36. (original) The formulation of claim 35 wherein the concentration of morphine, and amount and particle size of the formulation delivered from the device, is selected so that about 500 mcg/min of morphine is deposited in the lungs during inhalation.

37. (currently amended) A method of administering an opioid formulation to provide analgesia to a patient, comprising the steps of:

continuously inhaling the formulation using a pulmonary drug delivery device to produce analgesia; and

stopping inhalation when satisfactory analgesia is achieved or at the onset of a side effect;

wherein the formulation comprises either (1) fentanyl and liposomally encapsulated fentanyl or (2) the combination of (a) remifentanyl, alfentanil, sufentanil, or fentanyl and (b) methadone ~~an effective amount of at least one rapid-onset opioid and a pharmaceutically acceptable carrier~~; the concentration and type of each opioid, and amount of and particle size of the formulation delivered from the device on each inhalation, being selected so that, during inhalation, analgesia is achieved before the onset of said side effect, and the onset of said side effect occurs before the onset of toxicity, and so that the maximum total opioid plasma concentration does not reach toxic levels, whereby the onset of said side effect can be used by the patient to terminate inhalation to avoid toxicity.

38. (currently amended) The method of claim 37 wherein the pulmonary drug delivery device ~~comprises:~~

~~— a container containing said formulation;~~

~~— means for forming the formulation into particles having a mass medium aerodynamic diameter of from 1 to 5 microns for delivery to a patient;~~

~~— an outlet through which the formulation is dispensed; and~~

~~means for dispensing said formulation through said outlet;~~

~~wherein the device~~ is adapted to dispense the formulation only through an exercise of conscious effort by the patient.

39. (currently amended) A pulmonary drug delivery device comprising:

a container containing a formulation comprising an effective amount of either (1) fentanyl and liposomally encapsulated fentanyl or (2) the combination of (a) remifentanyl, alfentanil, sufentanil, or fentanyl and (b) methadone at least one rapid-onset opioid and a pharmaceutically acceptable carrier;

~~means for forming the formulation into particles having a mass-medium aerodynamic diameter of from 1 to 5 microns for delivery to a patient;~~

~~an outlet through which the formulation is dispensed; and~~

~~means for dispensing said formulation through said outlet;~~

wherein the device is adapted to dispense the formulation only through an exercise of conscious effort by the patient; and the concentration and type of ~~each~~ each opioid, and amount of and particle size of the formulation delivered from the device on each inhalation, is selected so that, during inhalation, analgesia is achieved before the onset of said side effect, and the onset of said side effect occurs before the onset of toxicity, and so that the maximum total opioid plasma concentration does not reach toxic levels, whereby the onset of said side effect can be used by the patient to terminate inhalation to avoid toxicity.

40. (cancelled) The device of claim 39 further comprising delivery rate controlling means for limiting the rate at which the formulation is dispensed to below a selected threshold.

41. (original) The device of claim 39 wherein said device has a weight ranging from 250 to 2500 grams.

42. (currently amended) The device of claim 39 further comprising an outlet through which the formulation is dispensed, wherein said outlet comprises a fenestration which must be sealed by the lips of the patient in order for the formulation to be dispensed.

43. (currently amended) The device of claim 39 wherein the dispensing of the formulation ~~said dispensing means is~~ breath actuated.

44. (currently amended) An opioid administration kit comprising:

a pulmonary drug delivery device comprising a container capable of containing a formulation; ~~means for forming a formulation contained in the container into particles having a mass medium aerodynamic diameter of from 1 to 5 microns for delivery to a patient;~~ an outlet through which the formulation is dispensed; ~~and means for dispensing said formulation through said outlet;~~ wherein the device is adapted to dispense the formulation through said outlet only through an exercise of conscious effort by the patient; and

an opioid formulation contained in the container or for receipt by the container, said formulation comprising an effective amount of ~~at least one rapid-onset opioid and a pharmaceutically acceptable carrier~~ either (1) fentanyl and liposomally encapsulated fentanyl or (2) the combination of (a) remifentanyl, alfentanil, sufentanil, or fentanyl and (b) methadone; the concentration and type of each opioid, and amount of and particle size of the formulation delivered from the device on each inhalation, being selected so that, during inhalation, analgesia is achieved before the onset of said side effect, and the onset of said side effect occurs before the onset of toxicity, and so that the maximum total opioid plasma concentration does not reach toxic levels, whereby the onset of said side effect can be used by the patient to terminate inhalation to avoid toxicity; and

instructions for using said kit comprising the steps of continuously inhaling the formulation using a pulmonary drug delivery device to produce analgesia;

and stopping inhalation when satisfactory analgesia is achieved or at the onset of a side effect.

45. (original) The kit of claim 44 wherein said instructions further comprises the step of filling the device with said opioid formulation prior to administration.

46. (cancelled) The use of a formulation according to claim 1 in the manufacture of a medicament for providing analgesia to a patient.

47. (cancelled) The use of a formulation according to claim 1 in providing analgesia to a patient.

48. (previously presented) An opioid formulation for use in a method of providing analgesia to a patient in a pulmonary drug delivery device, wherein the formulation comprises a rapid onset opioid, a sustained effect opioid, and a pharmaceutically acceptable excipient suitable for pulmonary administration, wherein the ratio of said two opioids is selected such that a combined pharmacokinetic profile of the opioids has a combined effect curve providing a peak concentration at an effect site at between 10 and 30 minutes and a concentration at the effect site of a magnitude of at least 85% of said peak concentration for at least 2 hours, and wherein the rapid onset opioid is selected from the group consisting of fentanyl, remifentanyl, alfentanil and sufentanil, and the sustained effect opioid is selected from the group consisting of morphine, and methadone.